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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 :
C12N 15/62, C07K 19/00, 14/82, 14/52, 14/78, 14/47, 16/18, 16/28, 16/44, C12N 1/21, 1/19, 5/10, A61K 38/17, 39/395, G01N 33/50 // (C12N 1/21,C12R 1:19)

A3

(11) International Publication Number: WO 96137621

(43) International Publication Date: 28 November 1996 (28.11.96)

(21) International Application Number: PCT/EP96/02230

(22) International Filing Date: 23 May 1996 (23.05.96)

(30) Priority Data:
95107914.4 23 May 1995 (23.05.95) EP
(34) Countries for which the regional or international application was filed: DE et al.

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(81) Designated States: CA, CN, JP, US, European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(88) Date of publication of the international search report:
3 January 1997 (03.01.97)

(54) Title: MULTIMERIC PROTEINS

(57) Abstract

The present invention relates to the construction and use of small multimerization devices, preferably of human origin, which self-assemble fused functional domains to multimeric and multifunctional complexes. Multimerization devices of this invention do not significantly interfere with secretion, expression yields and the independent folding of functional domains, which are attached via flexible but protease-resistant linkers. Modular gene cassettes encoding functional domains, linkers and multimerization domain can easily be combined to a cistron encoding the multimeric protein. Translation in a suitable host results in self-assembly to multimers larger than dimers. In cases, in which one or both functional domains are not expressible in sufficient yields or native fold in the same expression host, multimeric proteins can be produced, in which one or both functional domains or the multimerization device are produced separately by, e.g., in vitro translation, peptide synthesis and/or refolding and subsequently, e.g., chemically coupled to the remaining part of the multimeric protein.

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INTERNATIONAL SEARCH REPORT

Int. ional Applicahon No
PCT/EP 96/02230

4. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/62 C07K19/00 C07K14/82 C07K14/52 C07K14/78
C07K14/47 C07K16/18 C07K16/44 C07K16/28 C12N1/21
C12N1/19 C12N5/10 A61K38/17 A61K39/395 G01N33/50
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3. FIELDS SEARCHED

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IPC 6 C12N C07K A61K G01N

Documentahon searched other than minimum documentahon to the extent that such documents are included in the fields searched

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C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO,A,96 13583 (MORPHOSYS PROTEINOPTIMIERUNG ;PACK PETER (DE) ; LUPAS ANDREI (DE)) 9 May 1996 see figure 2 ---	1,25-37
X	J IMMUNOL METHODS, JAN 27 1995, 178 (2) P201-9, NETHERLANDS, XP000608189 DUBEL S ET AL: "Bifunctional and multimeric complexes of streptavidin fused to single chain antibodies (scFv)." see the whole document --- -/--	1,25-41

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Date of the actual completion of the international search	Date of mailing of the international search report
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Name and mailing address of the ISA	Authorized officer
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Inter nal Application No
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IPC 6 //(C12N1/21,C12R1:19)

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Electronic data base consulted during the international search (name of data base and, where prachcal, search terms used)

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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	WO,A,93 15210 (MERCK PATENT GMBH) 5 August 1993 cited in the application see page 10 - page 13; examples 1-4 ---	1-3, 12-16, 25-41
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Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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Int onal Application No
PCT/EP 96/02230

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